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04/30/2002 - Updated 09:22 PM ET

### Sizing up omega-3

By Nanci Hellmich, USA TODAY

What should you eat to get enough omega-3 fatty acids in your diet for a healthy heart?

Try eating salmon, sardines, herring, mackerel, trout or swordfish two or three times a week. If you can't stomach those, eat a tuna sandwich a couple of times a week with mayonnaise made with canola oil or soybean oil.

Once a day, you might cook with one of those oils. Or make your salads with those oils or flaxseed oil. Or for variety, try using walnuts or ground-up flaxseeds as a topping for your cereals, say some of the top nutrition researchers on these fats. Or you could take fish-oil supplements.

Scientists have been singing the praises of omega-3 fatty acids for years now. Research has shown that they reduce sudden death from heart attack probably by preventing fatal rhythm disturbances. Two studies, out in April, revealed that people with no heart trouble can safeguard their hearts and reduce their risk of sudden death by eating oily fish twice a week. Plus, other studies link omega-3 fatty acids to potential benefits for

#### Fish, other foods rich in fatty acids

Experts are divided on the amount of omega-3 fatty acids needed to get health benefits, but many recommend eating fish twice a week. Others also suggest eating plant foods rich in these fats. Here's a look at some foods high in omega-3 fatty acids:

- Fish
- Salmon
- Trout
- Tuna
- Lake whitefish
- Bluefish
- Swordfish
- Herring
- Anchovies
- Mackerel
- Sardines

Source: The Omega Diet; *Prevention Magazine's Complete Nutrition Reference Handbook*

#### Other resources:

- Flaxseed oil
- Walnuts
- Canola oil
- Soybean oil
- Mayonnaise
- Italian dressing made

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omega-3 fatty acids to potential benefits for the treatment of everything from depression to arthritis to colon inflammation.

Italian dressing made with soybean oil

Source: Eat, Drink, and Be Healthy.

But many questions remain unanswered, and, meanwhile, Americans are floundering about what they should be eating.

There still is no final word on how much omega-3 fatty acids a person should consume, but it is clear that many Americans are not getting enough, says Walter Willett, chairman of the department of nutrition at Harvard School of Public Health. He worked on the latest studies on this fat.

For someone who is basically healthy, just having fish several times a week will give most, if not all, of the benefits, he says. "It doesn't seem we need to be eating large amounts of fish every day," says Willett, author of *Eat, Drink, and Be Healthy*.

Studies in England, France, Italy and India show the benefits of these essential fats, says Artemis Simopoulos, one of the pioneer researchers in this area and author of *The Omega Diet: The Lifesaving Nutritional Program Based on the Diet of the Island of Crete* with Jo Robinson.

#### Not just in fish

Fish may be the richest source of long-chain omega-3 fatty acids, but plant foods such as flaxseeds, flaxseed oil, canola oil, unhydrogenated soybean oil and walnuts contain shorter-chain omega-3 fatty acids called alpha-linolenic acid. Some of those can be converted to the long-chain version, Willett says.

It takes about 10 grams of the shorter-chain version to make one gram of the long-chain version, Simopoulos says. Vegetarians and people who really don't like fish should try to add those plant foods to their diet, she says.

Simopoulos and Willett offer these other suggestions for enriching the diet in omega-3 fatty acids:

- Try to incorporate fatty fish into your diet two or three times a week. Besides the omega-3 fatty acid benefits, there are probably some additional advantages in having fish because it's often replacing red meat, which has other downsides, such as large amounts of saturated fat, Willett says.
- Eat your tuna. Simopoulos says many Americans don't like fish such as herring, sardines and salmon, but they will eat tuna, so she tells people to make their tuna salad with canola-oil mayo. Or use canned salmon, mackerel and herring, and make a salad in a similar way, she says. Willett says the tuna can be packed in spring water, soybean oil, canola oil or olive oil.
- Get at least one good source of alpha-linolenic acid most days, Willett says. Flaxseed and flaxseed oil provide the highest concentrations of short-chain omega-3 fatty acids. "Even a teaspoon of flaxseed oil a day would give you a lot. You could add it to a salad. I add a little flaxseed to my multi-grain cereal. It's better absorbed if you put it into a coffee grinder."
- Use mayonnaise and regular salad dressings that are made with canola or soybean oil, Willett says. "Ironically, many people have

eliminated their major source of omega-3 fatty acids by going to fat-free salad dressings," he says. (The regular versions are often higher in calories.)

- Cook with canola or olive oil, Simopoulos says.
- Eat walnuts. "They are a perfect food," she says.
- Try foods such as eggs and bread that have been enriched with omega-3 fatty acids, Simopoulos says.

### Omega-3 vs. omega-6

The omega-3 picture is muddled by theories about omega-6 fatty acids found in vegetable oils such as corn, safflower, cottonseed and sunflower oils. Simopoulos says people in the USA consume too many of these oils and need to eat a more balanced ratio of omega-6 to omega-3 fatty acids. She doesn't support eating soybean oil, she says, because it's too high in omega-6.

Willett says there is no evidence that the levels of omega-6 fatty acids consumed in the USA are harmful, and in fact, there is evidence of benefit.

He says people who have had a heart attack who are not going to eat fish regularly might want to take a supplement that contains one gram of omega-3 fatty acid. He says there may be some additional benefits from higher doses for the heart (keeping blood platelets from clumping together), but those benefits are small and more easily obtained by taking a baby aspirin daily or every other day.

Others believe people should consume higher doses of omega-3 fatty acids. Best-selling diet author Barry Sears, whose *The Omega Rx Zone* is out this month, doesn't think that fish twice a week provides enough omega-3 fatty acids necessary for all the potential health benefits. He recommends supplements that provide at least 2.5 grams per day. (He sells his brand of supplements.)

For those who do eat fish, shop carefully.

Farm-raised fish are less likely to be contaminated by mercury and other poisons than ocean-caught fish, but they may not be as high in omega-3 fatty acids, depending on what they were fed, Willett says. If the fish are fed other fish or algae, they will have a high content of omega-3 fatty acids, he says. But if they are fed wheat and corn, they won't contain as much.

"We need to be monitoring this," he says. "And it may well be that there needs to be a label that gives the omega-3 fatty acid content of farmed fish."

**Morgan Stanley**

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**EPA** (eicosapentaenoic acid) is an **omega 3** fatty acid with 20 carbons and five double bonds and this is found in fatty fish.


**DHA** (docosahexaenoic acid) **omega 3** fatty acid with 22 carbons and six double bonds and this is found in all fish and shell fish. It is likely that each **omega 3** fatty acid has different functions in the body.


When we eat **ALA** a small amount is converted to **EPA** and in certain tissues, such as the brain and the retina, some **ALA** is converted to **DHA**. If we eat fish, the **EPA** and **DHA** are taken up into body tissues very efficiently. Therefore, the best dietary sources of the **omega 3** fatty acids are from fish. On average Australians eat about 0.1 to 0.2 gram per day of **EPA** plus **DHA**, although for those who do not consume fish very often the amount is likely to be lower. To give an idea of amounts, consuming a 100 gram can of tuna (in water) provides about 0.2 gram of **EPA** plus **DHA**. It has been suggested on the basis of studies conducted around the world that the intake of these fatty acids should be more than double our current intake upper limit (even as much as 600 mg per day).

Vegetable oils containing **ALA** and fish oils containing **EPA** and **DHA** can have beneficial effects on the cardiovascular system and perhaps these fatty acids operate via different mechanisms.

 Recent studies have indicated that a higher dietary intake of **ALA** is protective against fatal Ischaemic Heart Disease in women (Hu et al Am J Clin Nutr 69:890-8 1999).

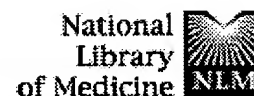
 Studies using mustard seed oil (contains **ALA**) or fish oil (**EPA** and **DHA**) demonstrate protective benefits against second heart attacks in men (Singh et al Cardiovasc Drugs & Therapy 11:485-491, 1997).

 Studies using **canola** oil (contains **ALA**) show improvements in arterial compliance, an important index of blood vessel health (Nestel et al Atheroscler Thromb Vasc Biol 17:1163-1170, 1997).

 The Lyon Diet Heart study supports the beneficial effects of diets rich in **ALA** (from **canola** oil) on secondary prevention of CVD (de Lorgeril et al Lancet 343:1454-1459, 1994).

Last Updated: November 27, 2001.

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### Mechanism for the antitumor and anticachectic effects of n-3 fatty acids.

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Dietary intake of the n-6 fatty acid (FA) linoleic acid (LA) has a strong growth-promoting effect on many rodent tumors and human tumor xenografts grown in immunodeficient rodents. n-3 FAs such as alpha-linolenic and eicosapentaenoic acids (EPAs), which differ from LA and arachidonic acid, respectively, by only a single double bond in the n-3 position, are recognized cancer chemopreventive and anticachectic agents. Understanding how this seemingly small structural difference leads to such remarkable functional differences has been a challenge. In a previous study, we showed that LA uptake, [3H]thymidine incorporation into DNA, and total DNA content were decreased in tissue-isolated hepatoma 7288CTC perfused in situ with arterial blood containing alpha-linolenic acid, EPA, or docosahexaenoic acids. The  $K_i$  for the inhibition of LA uptake and [3H]thymidine incorporation by alpha-linolenic acid was 0.18 and 0.25 mM, respectively. Here we show that the addition of alpha-linolenic acid or EPA to arterial blood inhibits tumor FA uptake, including LA, and the subsequent conversion of LA to the mitogen 13-hydroxyoctadecadienoic acid (13-HODE) in vivo and during perfusion in situ. [3H]Thymidine incorporation during perfusion in situ was also inhibited. Addition of 13-HODE to the arterial blood reversed the inhibition of [3H]thymidine incorporation but had no effect on FA uptake. These two n-3 FAs also inhibited FA transport in inguinal fat pads in vivo and during perfusion in situ in fed (FA uptake) and fasted (FA release) rats. The effects of EPA and talinolenic acid on transport of saturated, monounsaturated, and n-6 polyunsaturated FAs in hepatoma 7288CTC and inguinal fat pads during perfusion in situ were reversed by the addition of forskolin (1 microM), pertussis toxin (0.5 microg/ml), or 8-bromo-cyclic AMP (10 microM) to the arterial blood. We conclude that the antitumor and anticachectic effects of

n-3 FAs on hepatoma 7288CTC and inguinal fat pads in vivo result from an inhibition of FA transport. These inhibitions are mediated by a putative n-3 FA receptor via a Gi protein-coupled signal transduction pathway that decreases intracellular cyclic AMP. A specific decrease in LA uptake and its conversion to the mitogen 13-HODE causes the tumor growth inhibition.

PMID: 11016660 [PubMed - indexed for MEDLINE]

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The following Huntington's Disease Society Bulletin states, "... a website has listed misleading information ...". The HDSA bulletin refers to The Huntington's Disease Lighthouse website because it was the only website that suggested that EPA could treat HD. I am still waiting for the HDSA quote the misleading information or to issue a bulletin to retract the lie that this website has listed misleading information. Jerry 13-Apr-2001

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HDSA BULLETIN - RESEARCH 10/11/00

## HDSA BULLETIN - RESEARCH

Dear friend of HDSA:

It has come to our attention that a website has listed misleading information on a substance called **ethyl eicosapentaenoic acid, or ethyl-EPA**. The Huntington's Disease Society of America would like to provide the facts on this topic and dispel any confusion that may have been caused. Please pass this information on to people that you believe will be interested in Huntington's Disease research.

Ethyl eicosapentaenoic acid, or ethyl-EPA, is a 97% pure ethyl ester of EPA, and is also known as LAX-101. It is a chemically synthesized derivative of a pure highly unsaturated fatty acid. While EPA is found as a minor component of fish oil, LAX-101 (ethyl-EPA) is a single chemically-modified compound. The rationale for studying its effects on Huntington's Disease stems from the compound's ability to inhibit phospholipase A2, or PLA2. PLA2 is induced by cellular stress and causes damage to cell membranes. The mechanism of damage in Huntington's Disease is currently unknown, but it may be associated with excess activity of PLA2. Early pilot studies in a small number of patients showed improvements in some motor symptoms, as assessed by the **Unified Huntington's Disease Rating Scale (UHDRS)**. These initial studies on LAX-101 are interesting, but are far from proving its efficacy, and have not ruled out the possibility of side effects.

Laxdale, Ltd., of Scotland, is the company that is pursuing studies on their compound, LAX-101. The Huntington's Disease Society of America has been working with Laxdale to arrange for a Phase II clinical trial in the United States. This trial is vital in determining whether LAX-101 has efficacy in patients with HD. Laxdale has secured orphan drug status for LAX-101 and is awaiting a response on their investigational new drug (IND) application.



The HDSA Centers of Excellence at Johns Hopkins University and Emory University are slated to be the two U.S. sites taking part in this multi-center, international trial. (Other sites will be in Vancouver and England.) Once approvals have been finalized by the FDA and the institutional review boards of the sites, the trial will commence recruitment of participants.

This trial will be double-blind, and placebo-controlled, and eligible participants must be in stage I or II of Huntington's Disease. ('Double-blind' indicates that neither the investigator nor the patient know whether the patient is receiving the compound or the 'placebo' [inactive identical-appearing pill]). Recruitment of the 30-40 patients per site for a total of 160 patients in the study is estimated to start this fall. Laxdale estimates that results will be available before the end of 2002.

To date, there has not been a wealth of compounds progressing to clinical trials for HD. It is important that we as the HD community not jeopardize the integrity of any clinical trial; if misinformation is spread about a potential compound, the trial can be compromised. HD patients and families should note that fish oils have not been studied, nor have they shown efficacy in HD. Fish oils vary enormously in their composition. It is possible that fish oils will not be beneficial, and, without testing, a harmful effect cannot be ruled out. Patients who are taking fish oil (this can be determined by blood testing) will be excluded from the LAX-101 study by the investigators conducting the trial.

As it becomes available, HDSA will provide information on this trial in our upcoming newsletters and e-mail bulletins. If you would like to be notified of recruitment and contact information for this trial, please make sure that you are on our mailing list and receive our e-mail bulletins. To do so, send your contact information to [hdsainfo@hdsa.org](mailto:hdsainfo@hdsa.org) and indicate that you would like to receive bulletins.

HDSA's position statement on experimental or alternative therapies is as follows:

"Currently there is no clinically available pharmacological, biological, or surgical agent or method which slows or stops the progression of HD. In lieu of such a treatment, clinicians prescribe drugs or physical and behavioral interventions to ameliorate symptoms. HDSA recommends A Physician's Guide to the Management of Huntington's Disease, Second Edition as a source of information on currently used symptomatic and supportive therapies.

HDSA supports continued research to better understand HD, and in turn reveal potential new and experimental treatments. Some new experimental therapies are first tested in a study wherein all patients receive the actual medications. A more sophisticated study must be undertaken to determine if the medication actually works. A definitive therapeutic study must be a so-called "double masked" (also called "double-blind") trial that compares results in individuals who have taken the drug with individuals who have been given a placebo. A double-blind trial is one in which neither the physician nor the patient knows whether the patient is taking the active drug or placebo. Any research study must be accompanied by an informed consent statement to ensure that participants understand any possible risks and benefits. An appropriate Institutional Review Board (IRB) must review this informed consent statement.

HDSA advises that patients proceed with caution and seek the knowledge of their physician or specialist in understanding the risks and benefits associated with any therapies. HDSA does not recommend the use of drugs or other treatments that have not been proven safe and

effective in rigorous research studies for individuals with HD. Disease manifestation in HD patients is individual-specific and varies widely. We recommend that physicians provide their patients (and families/significant others) with detailed and personalized advice on the use of any alternative therapies. Conversely, it is important for patients to inform their physicians about any therapeutic agents or programs they are pursuing."

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